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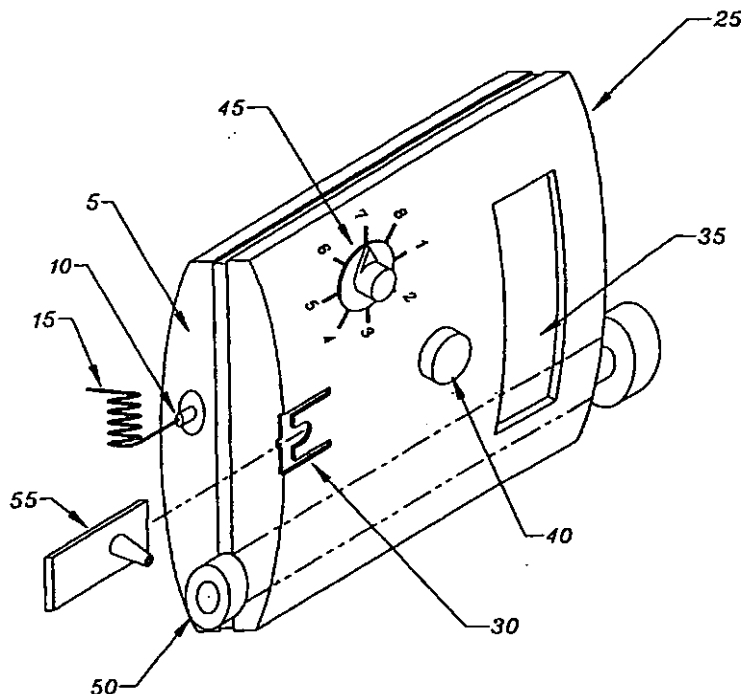
INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification ⁷ : A61B 5/00, A61M 5/172, G01N 33/487</p>	<p>A1</p>	<p>(11) International Publication Number: WO 00/13580</p> <p>(43) International Publication Date: 16 March 2000 (16.03.00)</p>		
<table style="width: 100%;"> <tr> <td style="width: 45%; vertical-align: top;"> <p>(21) International Application Number: PCT/US99/20978</p> <p>(22) International Filing Date: 10 September 1999 (10.09.99)</p> <p>(30) Priority Data: 60/099,894 11 September 1998 (11.09.98) US</p> <p>(71) Applicant (for all designated States except US): AMIRAL MEDICAL [US/US]; 4742 Scotts Valley Drive, Scotts Valley, CA 95066 (US).</p> <p>(72) Inventors; and (75) Inventors/Applicants (for US only): YUM, Su, I. [US/US]; 1021 Runnymede Court, Los Altos, CA 94024 (US). DOUGLAS, Joel, S. [US/US]; 25285 La Loma Drive, Los Altos, CA 94022 (US). ROE, Jeffrey, N. [US/US]; 3212 Vera Cruz Drive, San Ramon, CA 94583 (US).</p> <p>(74) Agent: COVERSTONE, Thomas, E.; Burns, Doane, Swecker & Mathis, LLP., P.O. Box 1404, Alexandria, VA 22313-1404 (US).</p> </td> <td style="width: 55%; vertical-align: top;"> <p>(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p>Published With international search report.</p> </td> </tr> </table>			<p>(21) International Application Number: PCT/US99/20978</p> <p>(22) International Filing Date: 10 September 1999 (10.09.99)</p> <p>(30) Priority Data: 60/099,894 11 September 1998 (11.09.98) US</p> <p>(71) Applicant (for all designated States except US): AMIRAL MEDICAL [US/US]; 4742 Scotts Valley Drive, Scotts Valley, CA 95066 (US).</p> <p>(72) Inventors; and (75) Inventors/Applicants (for US only): YUM, Su, I. [US/US]; 1021 Runnymede Court, Los Altos, CA 94024 (US). DOUGLAS, Joel, S. [US/US]; 25285 La Loma Drive, Los Altos, CA 94022 (US). ROE, Jeffrey, N. [US/US]; 3212 Vera Cruz Drive, San Ramon, CA 94583 (US).</p> <p>(74) Agent: COVERSTONE, Thomas, E.; Burns, Doane, Swecker & Mathis, LLP., P.O. Box 1404, Alexandria, VA 22313-1404 (US).</p>	<p>(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p>Published With international search report.</p>
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(54) Title: **DEVICE FOR DETERMINATION OF AN ANALYTE IN A BODY FLUID INTERGRATED WITH AN INSULIN PUMP**

(57) Abstract

A combined blood glucose meter and insulin pump is disclosed, comprising a housing, a meter display visible from the outside of the housing, and at least one test strip that is stored in the housing. In an alternative embodiment, the combined blood glucose meter and insulin pump further comprise an optics system to receive colorimetric data from the test sample.



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-1-

DEVICE FOR DETERMINATION OF AN ANALYTE IN A BODY FLUID INTEGRATED WITH AN INSULIN PUMP

FIELD OF THE INVENTION

The present invention relates to a test device and determination of a
5 chemical or biochemical component (analyte) in an aqueous body fluid,
such as whole blood and an infusion system for delivering a chemical
therapy to a patient. In particular the present invention relates to an infusion
system integrated with an electronic system using a dry reagent test strip from
which an analyte presence and/or concentration is determined by use of an
10 instrument. A common use of such test strips is for determination of glucose level
in blood by diabetics and the delivery of insulin based on the glucose result.

BACKGROUND OF THE INVENTION

Numerous devices have been developed to test for presence and quantity of
analytes in aqueous samples, such as whole blood or urine. The patent and
15 technical literature of the last thirty years is replete with inventions which utilize a
reagent strip containing a dry chemistry reagent system, that is, a system in which
the wet chemistries are imbibed into an absorbent or bibulous medium, dried, and
later reconstituted by fluid from the test sample. The reagent strips contain an
indicator which changes color or a chemical system which produces an electrical
20 signal proportional to the presence or concentration of a particular analyte in a
biological fluid applied to the strip. These strips may be read colorimetrically by

-2-

an instrument calibrated or programmed to detect a certain color or by amphotometrically or coulombic means. Although some of these strips use reduction chemistries, more commonly they involve an oxidizable dye or dye couple. Some of the strips include an enzyme, such as glucose oxidase, which is capable of oxidizing glucose to gluconic acid and hydrogen peroxide.

The patient may also use an automated system to deliver drug therapy, such as insulin in diabetics. These systems are normally referred to as infusion pumps and are used to deliver such agents as insulin. The patient will use a diagnostic instrument and test strip to determine their analyte level and will then determine the appropriate therapy change and modify the delivery dosage of their infusion pump. However, this requires the patient to maintain and carry two separate devices, such as a monitoring system and an insulin delivery infusion pump. (See, for example, U.S. Pat. No. 4,935,346, to Phillips et al.) Examples of these devices, in addition to those used to test blood glucose, include tests for cholesterol, triglycerides, calcium or albumin in whole blood, and for protein, ketones, albumin or glucose in urine.

The Diabetes Complications and Control Trial, which was a study sponsored by the NIH, demonstrated conclusively that careful control of blood glucose levels can significantly reduce the incidence of serious complications of diabetes such as vision loss and kidney malfunction. Most diabetics must test themselves periodically in order to make appropriate adjustments to their diet or medication. It is therefore especially important for diabetics to have rapid, inexpensive, and accurate reagent strips for glucose determination. The convenience of having both the insulin delivery and monitoring system in one easy to use and carry unit will help provide an incentive for the patient to monitor and adjust their therapy appropriately to improve their condition.

-3-

The technologies embodied in the products which have been developed to date have certain limitations from the perspective of the end user and/or the manufacturer. There is, therefore, a need to overcome some of the limitations of currently available testing and infusion systems.

5 U.S. Pat. No.4,935,346, issued to Phillips. et al., discloses a system wherein a whole blood sample is applied to the device and indicator development occurs in the presence of the colored components of the sample. Measurements of the color change in the indicator are made at two distinct wavelengths to eliminate the interferences from the presence of colored blood components. The unit is of
10 considerable size and requires up to 12 μ of sample to perform a test.

Numerous electrochemical testing systems and related methods are known in the art. For example, European Patent Publication No.0255291 B I, to Birch et al., describes methods and an apparatus for making electrochemical measurements, in particular but not exclusively for the purpose of carrying out microchemical
15 testing on small liquid biological samples of clinical origin.

European Patent Publication No.0 351 891 B 1, to Hill et al., teaches a method of making an electrochemical sensor by printing. The sensor is used to detect, measure or monitor a given dissolved substrate in a mixture of dissolved substrates, most specifically glucose in body fluid.

20 U.S. Patent No.5,391,250, to Cheney II et al., teaches a method of fabricating thin film electrochemical sensors for use in measuring subcutaneous or transdermal glucose. Fabrication of the sensors comprises placing a thin film base layer of insulating material onto a rigid substrate. Conductor elements for the sensors are formed on the base layer using contact mask photolithography and a
25 thin film cover layer.

-4-

U.S. Patent No. 5,437,999, to Diebold et al., teaches a method of fabricating thin film electrochemical devices which are suitable for biological applications using photolithography to define the electrode areas. The disclosures of each of the above patent specifications are incorporated herein by reference in
5 their entirety.

Various infusion pump systems have been described in the current art and include U.S. Patent No. 4,704,029, to Van Heuvelen, which teaches a blood glucose monitor which is applicable for use as an implantable unit for controlling an insulin pump.

10 U.S. Patent No. 4,436,094, to Cerami, teaches a method for continuous monitoring of the glucose concentration which can be tied to an infusion device.

U.S. Patent No. 5,062,841, to Siegel, teaches an implantable self-regulating mechanochemical insulin pump.

15 U.S. Patent No. 5,665,065, to Colman et al., teaches a medication infusion device with a blood glucose data input method.

U.S. Patent No. 5,383,865, to Michel, teaches a medication dispensing device comprising an injector attached to a cartridge with a drive mechanism.

U.S. Patent No. 5,176,644, to Srisathapat et al., discloses a medication infusion pump with a simplified pressure reservoir.

20 The disclosures of the above patents are incorporated herein by reference.

-5-

The prior-art devices and methods of the above references provide varying degrees of effectiveness of blood analysis and drug infusion at varying degrees of complexity.

5 It is an object of the present invention to provide improved devices and methods to improve the performance and minimize the complexity compared to the prior-art devices.

It is a further object of the present invention to provide an integrated infusion pump and monitoring system.

10 It is another object of this invention to provide an integrated infusion pump, sampling system and monitoring system.

The above objects as well as others are achieved by die devices, methods and systems of this invention as disclosed herein.

SUMMARY OF THE INVENTION

15 In one aspect this invention provides a method of sampling a body fluid and applying the sample to a test strip which is either inserted or removed from the test strip holder located on the analyte testing portion of a combined insulin pump and glucose monitoring system. Wizen the test strip is positioned in the glucose monitoring system, the system then reads the analyte concentration and displays a value for that reading on a display located on the combined device.

20 In a preferred embodiment of the invention the device consists of a combined insulin delivery pump, blood glucose monitoring device and lancing system for the extraction of a blood sample. The system provides a small

-6-

convenient package which eliminates the need for the patient to carry three separate devices.

5 In a next preferred embodiment of this invention the device has a storage compartment for test strips to protect them from damage due to physical stress, moisture or light.

In another embodiment of this invention the device consist of a combined blood glucose meter and insulin pump.

10 The method comprises applying a blood sample to the test strip and reading the glucose concentration from the meter display. The display can be shared by the insulin delivery system or separate depending on the design of the instrument. The insulin delivery system settings are either modified by the patient or an algorithm in the electronic system calculates the system settings. This permits the fluid to pass through the capillary spreading layer/filter into the membrane, then reading or measuring on the test side of the membrane the
15 indication provided by the indicator of the presence or concentration of the analyte.

The above embodiments of the devices of the invention with the appropriate dry chemistry system in the matrix member can be used in test strips which may be read or measured in an electronic meter.

20 The above sets forth the generic aspects of the various devices and methods of the present invention. These devices and methods are more fully described in the drawings and the descriptions below.

-7-

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is an isometric view an insulin pump and combined test device.

Figure 2 is an isometric view of the insulin pump, test device, lancing system and test strip.

5 Figure 3 is a block diagram of the system components for a combined meter and insulin pump.

DETAILED DESCRIPTION OF THE INVENTION

10 The devices of the present invention are simpler to use and are easier and less costly to manufacture than most devices previously available. This is especially important for diabetics who rely on blood glucose testing multiple times per day to keep their disease under control.

 The ease of use and portability of these devices will facilitate increased patient compliance with recommended testing routines and will result in improved overall health of diabetic patients.

15 In one or more aspects of this invention an insulin pump is integrated with a blood glucose monitoring device to create a more portable and compact system for use by persons with diabetes. The embodiments can have the following characteristics, the first being a microprocessor which controls both the insulin delivery system and the blood glucose detection system, or a second type of device
20 which has two completely separate subsystems for insulin delivery and blood glucose monitoring but which are housed in the same case. Each of these solutions can be coupled with various case configurations to support integrated sampling

-8-

Systems and/or strip storage. The system could also support the necessary logic to link the blood glucose reading to an output which controls the insulin delivery of the pump to the patient.

5 The invention uses two categories of devices as noted above to solve the need for compact and discrete device for the treatment and monitoring of intensive therapy. By providing a feedback and software means to vary the insulin delivery to the patient based on the blood glucose reading, inputted exercise, and other factors, the diabetic patient is freed from many error-prone treatment determinations.

10 The integration of a blood glucose monitoring system and an insulin pump system can provide numerous benefits to the patient, one being the compact package, another the possibility of integrated algorithm, and still another the integrated sampling system and strip storage. These features provide portability and discreteness features not found in other devices and permit a possibility of a
15 semiclosed loop system.

The various aspects of the invention disclosed herein can best be illustrated by reference to the drawings and the description thereof which follows.

Figure 1 shows insulin pump 5 with catheter connection 10 and catheters
15 incorporated in a case 20 which has blood glucose monitor 25, strip holder 30,
20 and common display 35. The figure also shows the blood glucose monitor start button 40 and insulin pump dispensing selection button 45.

Figure 2 shows insulin pump 5 with catheter connection 10 and catheters
15 incorporated in a case 20 which has blood glucose monitor 25, strip holder 30, and common display 35. The figure also shows the blood glucose monitor start

-9-

button 40 and insulin pump dispensing selection button 45. A sampling system 50 used to extract a small sample of capillary blood is built into the unit and test strip 55 is used to collect and test the blood sample.

Figure 3 is a block diagram of the system components for a combined
5 meter and insulin pump. Insulin pump 5 is comprised of microprocessor 100,
metering pump 105 and indicator scales 110. The dispensing button 45 is used to
set the dispensing rate and time increment of the insulin dose. The serial
communication line 115 is used to connect the microprocessor 100 to the blood
glucose meter microprocessor 200. The blood glucose meter 25 has a
10 microprocessor 200 which runs the blood glucose meter and controls the common
display 35. The blood glucose start button 40 provides for the initiation of the
testing cycle used by the blood glucose monitor. The optics system 210 receives
colormetric data from the test and converts it to electrical signal in the analog to
digital circuit 215. The microprocessor 200 communicates with microprocessor
15 100 through the serial link 220. The serial link 220 permits the use of a common
display 35.

-10-

Claims:

- 1 1. A combined blood glucose meter and insulin pump, comprising:
2 a housing;
3 a meter display visible from the outside of said housing; and
 at least one test strip that is stored in said housing.
- 1 2. The combined blood glucose meter and insulin pump of Claim 1,
2 wherein the insulin settings are manually operated by the patient.
- 1 3. The combined blood glucose meter and insulin pump of Claim 1,
2 wherein the insulin settings are calculated by an electronic system utilizing an
3 algorithm.
- 1 4. The combined blood glucose meter and insulin pump of Claim 1,
2 further comprising:
3 a lancing system for obtaining the test specimen.
- 1 5. The combined blood glucose meter and insulin pump of Claim 3,
2 wherein said electronic system utilizing an algorithm is a microprocessor.
- 1 6. The combined blood glucose meter and insulin pump of Claim 5,
2 wherein said microprocessor controls the insulin delivery and the blood glucose
3 detection.
- 1 7. The combined blood glucose meter and insulin pump of Claim 5,
2 further comprising:
3 software means to provide feedback to vary the insulin delivery based on
4 the blood glucose reading.

-11-

1 8. The combined blood glucose meter and insulin pump of Claim 1,
2 further comprising:
3 a catheter connection to said housing.

1 9. The combined blood glucose meter and insulin pump of Claim 1,
2 further comprising:
3 an optics system to receive colorimetric data from the test sample.

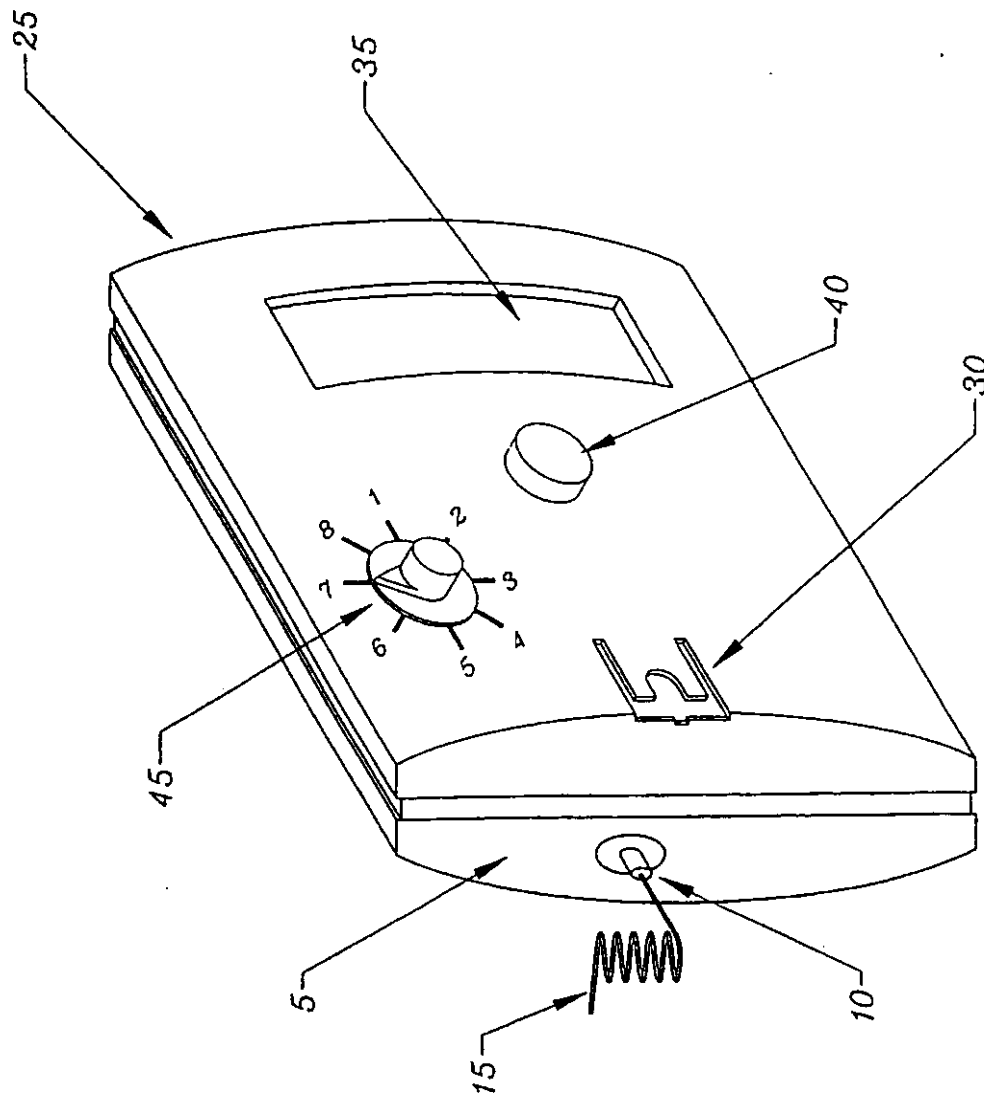
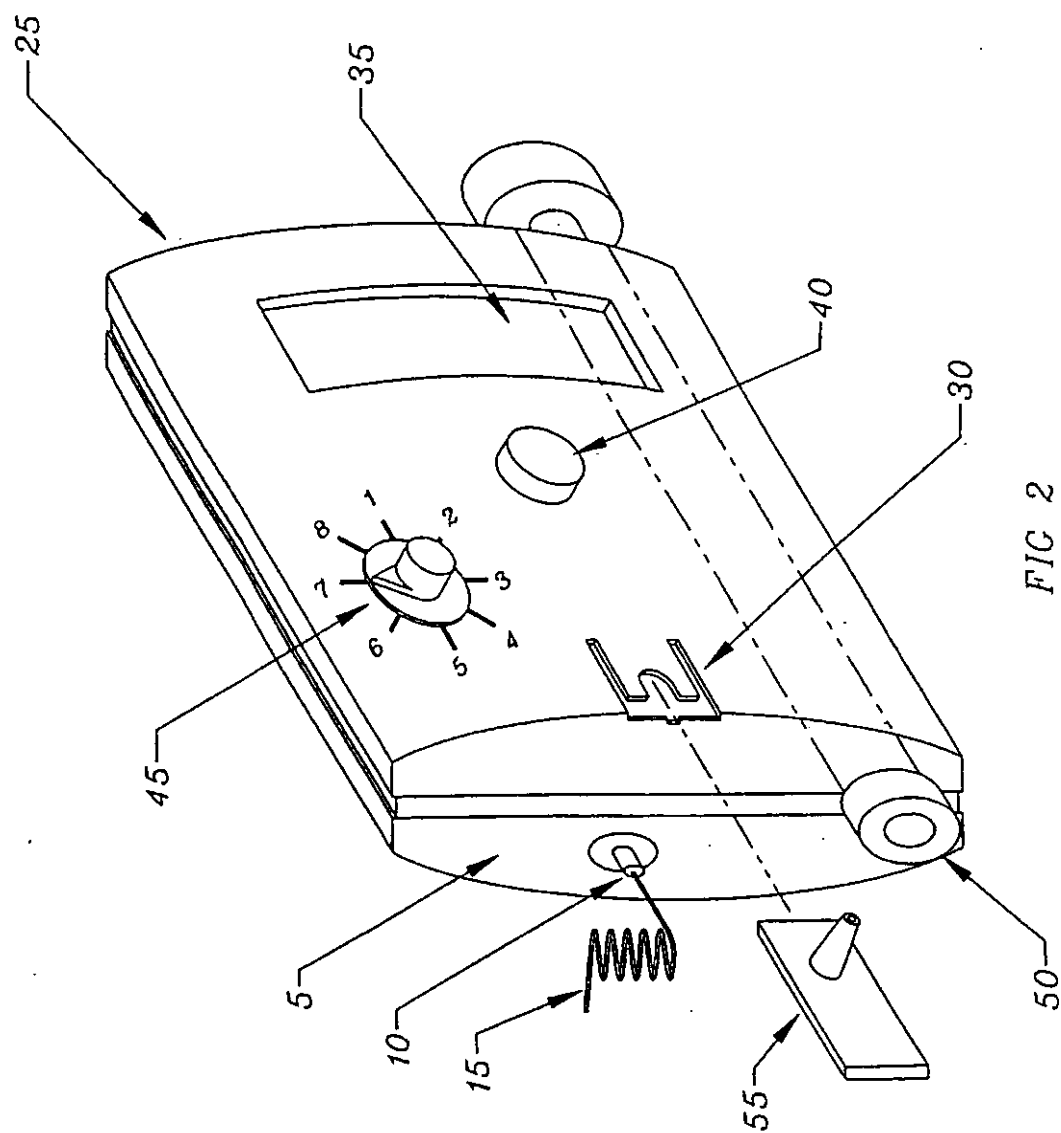


FIG 1



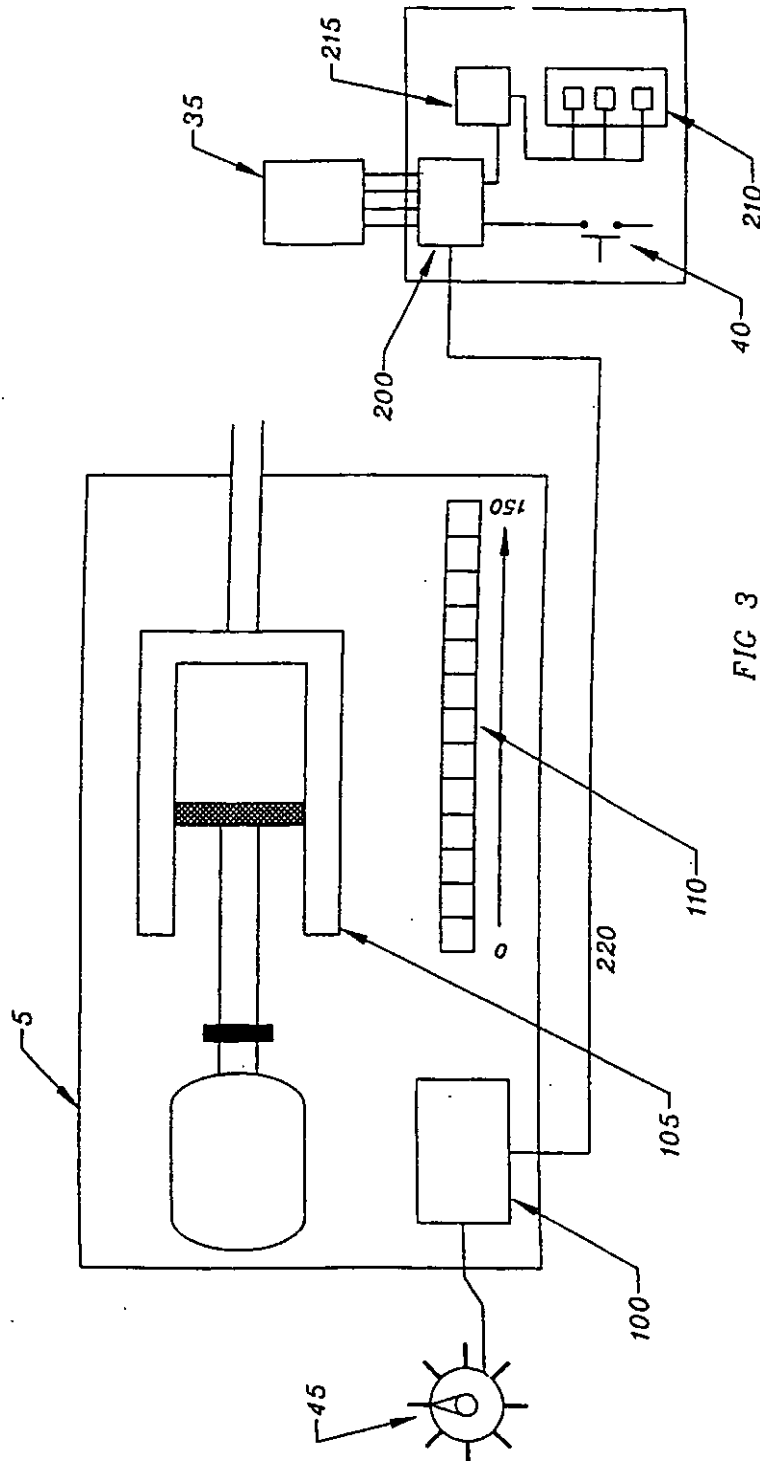


FIG 3

INTERNATIONAL SEARCH REPORT

Int. Patent Application No.
PCT/US 99/20978

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61B5/00 A61M5/172 G01N33/487

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61B A61M G01N

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C. DOCUMENTS CONSIDERED TO BE RELEVANT

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Y	column 16, line 53 -column 18, line 36 column 23, line 11 -column 26, line 20 column 27, line 24 - line 44; figures 14,15,25,26	1,3,5-7, 9
Y	EP 0 098 592 A (FUJISAWA PHARMACEUTICAL CO) 18 January 1984 (1984-01-18) page 7, line 15 -page 12, line 9 page 16, line 12 -page 18, line 9; figures	1,3,5-7, 9
A	US 5 665 065 A (COLMAN FREDRIC C ET AL) 9 September 1997 (1997-09-09) column 3, line 49 -column 5, line 40; figures	1-9
	-/-	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Manschot, J

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DE 42 34 553 A (FRESE VOLKER ;FRESE GOEDDEKE BEATE (DE)) 22 April 1993 (1993-04-22) the whole document	1,4

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/20978

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